

To Cite:

Dhok A, Chude S, Lakhani A, Onkar P, Mane P, Jakotia Y. Diagnostic accuracy of real-time shear wave elastography in the evaluation of prostatic lesion. Medical Science, 2023, 27, e143ms2094. doi: <https://doi.org/10.54905/disssi/v27i133/e143ms2094>

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Peer-Review History

Received: 02 October 2022

Reviewed & Revised: 06/October/2022 to 09/March/2023

Accepted: 12 March 2023

Published: 15 March 2023

Peer-review Method

External peer-review was done through double-blind method.

URL: <https://www.discoveryjournals.org/medicalscience>



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Diagnostic accuracy of real-time shear wave elastography in the evaluation of prostatic lesion

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ABSTRACT

This research aims to compare the diagnostic accuracy of ultrasound elastography to histology in evaluating prostate masses and assess its ability to distinguish malignant from benign diseases. The research involved 60 individuals with elevated PSA values (> 4 ng/ml) and aberrant DRE results were sent to our department. The trial lasted from August 2020 until February 2022. All patients gave informed consent and were aware of the potential complications of the biopsy. All the patients had B mode. Transrectal Ultrasonography, colour Doppler imaging, and transrectal real-time strain elastography were performed. The final diagnosis was confirmed with histopathological examination. The institutional ethics committee approved the study, and all patients obtained informed consent. In our study, the strain ratio has a sensitivity of 81.4%, a specificity of 83%, a positive predictive value of 88.4%, a negative predictive value of 83.5%, and an accuracy of 91.5% when a cut-off point of 5 is used to differentiate benign from malignant lesions. According to our results, prostate Ultrasonography coupled with elastography could be a valuable method for diagnosing malignant lesions and helps in targeting biopsy.

Keywords: Prostatic cancer, Transrectal biopsy, Ultrasound elastography, Strain ratio

1. INTRODUCTION

Prostate cancer is the second most common type of cancer in males globally (after lung cancer), accounting for 1,276,106 new cases and 358,989 mortality (3.8% of all cancer-related deaths in men) in 2018 (Bray et al., 2018), with prevalence anticipated to quadruple by 2030 (Bray and Piñeros, 2016; Kovács and Hoskin, 2013; Barr et al., 2017). In India prostate cancer has an incidence rate of 3.9 per 100,000 men, with 25,696 new cases and is responsible for 9% of all cancer related mortality (Hedgire et al., 2012). Traditionally, prostate cancer was detected with a digital rectal examination (DRE) and serum prostate specific antigen (PSA) measurement, followed by biopsy to confirm any suspicion (Eusebi et al., 2021).

Strain elastography (SE) and shear-wave elastography are two types of ultrasound elastography used to evaluate tissue elasticity in the prostate (SWE). The change in the elasticity of the prostate gland forms the basis for the identification of prostate diseases and this technique explores this very fact (Junker et al., 2014). To estimate the tissue stiffness of prostate, the most widely used technique is Strain elastography. Elastograms are obtained by manually compression and decompression the prostate using a transrectal probe. The images are color-coded to depict the spectrum of tissue elasticity, extending from red (soft tissue) to blue (hard tissue) (Junker et al., 2014). Through the use of TRTE-guided biopsy in medical practice, regions that are hard and have a diameter of 5 mm on elasticity imaging may be deemed malignant. Thus, the TRTE score, which is based on the symmetry and elastic distribution of the prostate, aids in both diagnosis and guided targeted biopsy.

Typically, prostate cancer is a firm lesion. A technique capable of mapping the prostate's elasticity may be beneficial in discovering and diagnosing malignant areas inside the prostate gland. The information obtained by ultrasound elastography on the stiffness of prostate tissue should aid in the diagnosis of prostate cancer and offer advice for tissue biopsy.

The aim of this prospective research is to determine the function of transrectal ultrasonography in the assessment of prostate cancer and the use of elastography in localising and targeting biopsy from suspicious lesions in a clinical setting utilizing pathological diagnosis as the gold standard.

2. MATERIALS AND METHODS

Data collection

The research comprised 60 patients referred to our department centre with increased PSA levels (>4 ng/ml) and aberrant DRE results. The research was conducted between September 2020 and February 2022 after getting permission from the Institutional Ethics Committee (IEC-18/2020). All patients gave informed consent and were informed of the potential complications of biopsy. Antibiotics were administered prophylactically prior to the surgery. Transrectal ultrasonography, transrectal real-time strain elastography, and biopsy were all performed at the same sitting on all patients. Histopathological investigation supported the final diagnosis.

Transrectal ultrasonography of the prostate was performed utilising a Samsung RS-80A equipped with an endocavitary transducer with a frequency range of 9-4 MHz and a field - of - view of 174 degrees capable of user selectable multi hertz imaging. On the probe that would be covered with the cover, lidocaine gel was administered. All patients were examined on their left side in the lateral decubitus posture, which was well tolerated. The prostate was scanned in grey scale in both axial and sagittal planes and the volume, echogenicity, surface, calcification, vascularity, and presence of nodules were all assessed. The size, position inside the gland, shape, echogenicity, border, and extension of each of these nodules were determined.

Ultrasound Elastography was done concurrently with the ultrasound examination using the Samsung RS80A and the same probe utilised for transrectal ultrasonography. We performed transrectal real-time strain elastography on the prostate.. The ultrasound probe is placed directly over the lesion, and the image is acquired in the screen's centre. The prostate was gently compressed and decompressed to get the elastogram. At least about 5 mm of normal adjacent tissue was included, and the lesion stiffness was calculated in proportion to the average elasticity of the surrounding tissue. Kamoi et al., (2008) proposed a grading system for target lesions.

The prostate was sampled in two planes, namely sagittal and the axial planes. Biopsies were performed with the use of a biopsy cannon (18 G 25 cm). A 12-core extended core biopsy procedure was employed. After obtaining biopsy samples, they were preserved in a 38 % formaldehyde solution and submitted to the histopathology laboratory for examination. If lesions are identified, targeted biopsy specimens acquired under TRUS and elastography guidance are delivered to the histopathology department in two different containers.

The Gleason score was used to grade the aggressiveness of prostate cancer. The histopathologist evaluated two tissue samples obtained from different areas of the prostate and assigned a score of 1 to 5 to each sample. The Gleason score was calculated as the sum of the two maximum values. Post-procedure, a few minor complications were observed and treated. Consent was obtained in accordance with the Ethics committee's guidelines. Between September 2020 and February 2022, we gathered histopathology findings from an electronic medical record system.

Criteria for inclusion

Raised PSA level

Abnormal findings discovered on digital rectal examination

Patients who have previously had negative biopsies and still have a strong suspicion for prostate cancer

Criteria for exclusion

Severe hemorrhagic diatheses

Bowel inflammation

Surgical amputation of the rectum and formation of anileo-anal pouch

Anticoagulant-treated patients having an international normalised ratio (INR) greater than 1.3

Patients who have refused to agree and are unwilling to undergo biopsy

Statistical analysis

Microsoft Excel and Epi info software tools were used to conduct the analysis. For quantitative data, the arithmetic mean \pm SD (or median) was used, but for qualitative (categorical) data, the frequencies (%) were used. $P < 0.05$ were considered significant. ANOVA, T-test, and two proportion Z test were employed as required to compare categorical variables (i.e. to investigate the connection between qualitative/quantitative variables).

3. RESULTS

Sixty patients with elevated PSA and abnormal DRE were examined using transrectal ultrasound, transrectal real time strain elastography, transrectal systematic core biopsies, and extra targeted biopsies from pathological regions detected by transrectal real time strain elastography and transrectal ultrasound, and the findings of these individual modalities were compared with histopathological findings as gold standard and results are as follows. 60% of the patients belonged to age group was 61-70 years followed by 71-80 years (31.66%). Age group for more than 80 yrs. include 3 out of 60 patients (5%) and for the age group < 50 and 51-60 years include 1-1 patient(1.7%). Mean value of age (years) of study subjects was 67.81 ± 9.32 with median (IQR) of 69.82 (61.2-75.9) and range of 37-86 as shown in table 1.

Table 1 Distribution of age (years) of study subjects

Age group	Frequency (n)	Percentage (%)
<50 years	1	1.7%
50 - 60 years	1	1.7%
61-70 years	36	60%
71-80 years	19	31.66%
>80 years	03	5%
Mean (SD)	67.81 (9.32)	
Median	69.82 (61.2-75.9)	
Range	37-86	

The mean PSA (ng/mL) level for malignancy was 55.23 with a standard deviation of 29.98 and the mean PSA (ng/mL) level for benign pathologies was 7.43 ng/mL with a standard deviation of 4.16. However the overall mean value of PSA(ng/mL) of study subjects is 39.2 ± 11.76 with median (IQR) of 41.54(2.57-112.2). Similarly the mean PSA density (ng/cm³) level for malignancy was 1.38 with a standard deviation of 0.73 and the mean PSA density (ng/cm³) level for benign conditions was 0.28 ng/mL with a standard deviation of 0.46. However, the overall mean value of PSA density (ng/cm³) of study subjects is 0.631 ± 0.248 with median (IQR) of 0.714 (0.05-3.33) (table 2).

Table 2 PSA volume and density distribution in type of neoplasia diagnosis using ultrasound elastography as diagnostic tool

PSA Volume	Mean	S. D	Unpaired 't' test	p value
Benign Rx Ultrasound	7.43	4.16	t =10.097	p<0.001**
Malignant Rx Ultrasound	55.23	29.98		
	Mean (SD)	39.2(11.76)		
	Median	41.54		
	Range	2.57-112.2		
PSA Density	Mean	S. D	Unpaired 't' test	p value

Benign Rx Ultrasound	0.28	0.46	t =7.072	p<0.001**
Malignant Rx Ultrasound	1.38	0.73		
	Mean (SD)	0.631 ± 0.248		
	Median	0.714		
	Range	0.05-3.33		

The mean size prostate for malignancy was 47.68 cm³ with a standard deviation of 8.63 and the mean size of prostate for benign conditions was 42.6 cm³ with a standard deviation of 5.68. However, the overall mean size of prostate in our study is 44.2 ± 6.5 with median (IQR) of 42.87(30-65). The mean strain ratio for benign is 2.86 and for malignancy is 5.86 as shown in table 3 and figure 1.

Table 3 TRUS volume comparison in type of neoplasia diagnosis using ultrasound elastography as diagnostic tool

TRUS VOLUME	Mean	S. D	Unpaired 't' test	p value
Benign Rx Ultrasound	42.6	5.68	t = 2.713	p =0.009*
Malignant Rx Ultrasound	47.68	8.63		
	Mean (SD)	44.21(6.54)		
	Median	42.87		
	Range	30-65		

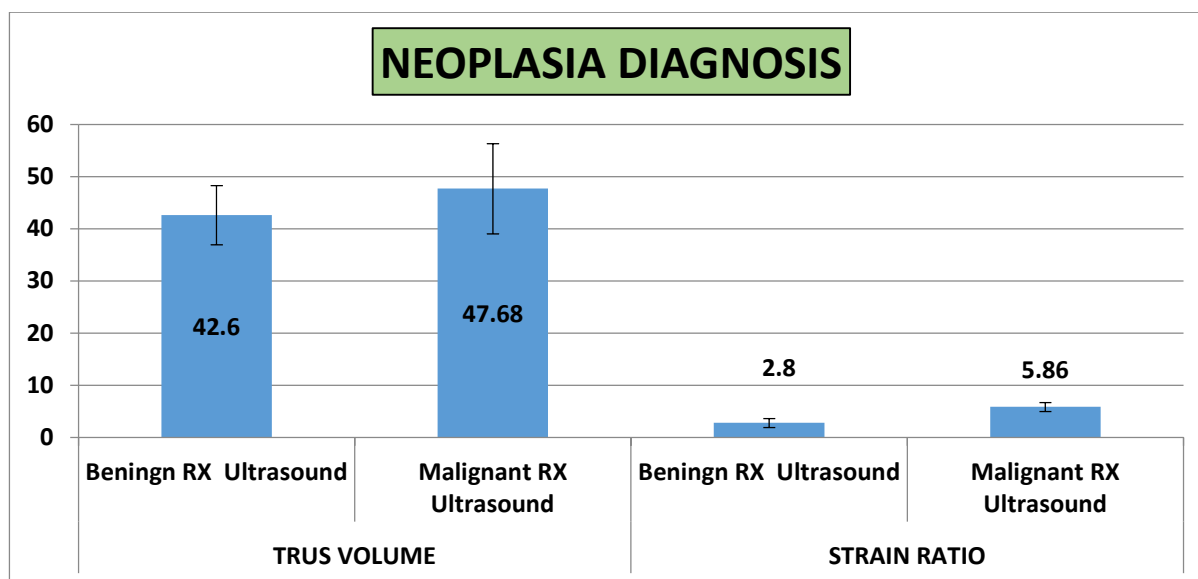


Figure 1 TRUS volume and strain ratio comparison in type of neoplasia diagnosis using ultrasound elastography as diagnostic tool.

TRUS (Transrectal Ultrasound) features such as uniform echogenicity, hypoechoic, hyperechoic and capsular irregularity were considered. Out of 60 cases 21 lesions suspicious of malignancy were examined on TRUS. Out of these 21 cases, 16(76.2%) were correctly identified as malignancy while 5(23.8%) proved to be benign lesions. TRUS was not successful to identify 5 (23.8%) malignant lesions were turn out to be benign lesions as shown in table 4.

Table 4 Characterization of Lesion by Using Ultrasound Elastography as Diagnostic Tool

	Frequency (n)	Percentage (%)
Uniform echogenicity	29	48.3%
Hypoechoic Lesion	19	31.7%
Hyperechoic Lesion	12	20%

Out of 60 cases 39 lesions were negative for malignancy was identified on TRUS. Out of these 39 cases, 37(94.9%) were correctly identified as negative malignant lesion turn out to be benign while 2(5.1%) turned out to be malignant lesions. TRUS failed to identify 2(5.1%) lesions as a negative lesion were turn out to be malignant (table 5).

Table 5 Transrectal ultrasound findings in correlation with histopathology

TRUS FINDINGS	HISTOPATHOLOGY	
	BENIGN	MALIGNANT
NEGATIVE FOR MALIGNANCY (n=39)	37 (94.9%)	2 (5.1%)
POSITIVE FOR MALIGNANCY (n=21)	5 (23.8%)	16 (76.2%)
Total	42	18

In the present study Out of 60 cases 21 lesions doubtful of malignancy were identified on TRUS. On histopathology out of these 21 cases, 16(88.9%) were correctly identified as malignancy while 5(11.9%) turned out to be benign lesions. 20 cases were classified under Elastography grade III. On histopathological evaluation, 13 (31%) out of 20 cases were benign. 7 (38.9%) out of 20 cases were malignant. Another 8 cases were classified under Elastography grade IV. On histopathological evaluation, 7 (38.9%) out of 8 cases were turn out to be malignant as adenocarcinoma of prostate and 1(2.4%) case is benign. Another 3(16.7%) were strongly suspicious to be malignant on elastography V and all of them turned out to be adenocarcinoma of prostate on histopathological evaluation (figure 2 - 4).

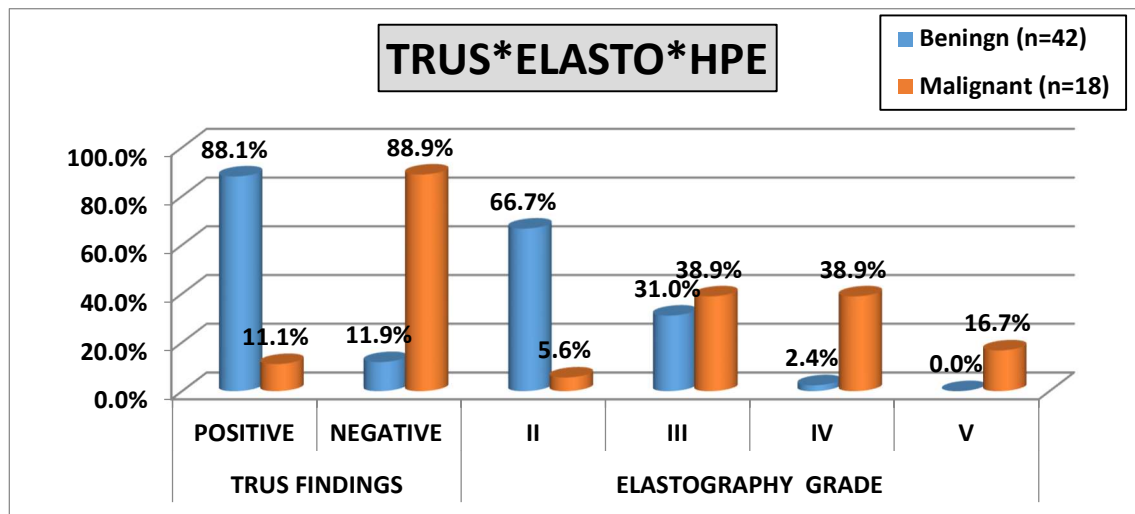


Figure 2 Correlation of TRUS, Elastography Grade with histopathological diagnosis

Table 6 Use of strain ratio in diagnosing lesion of Prostate

Strain Ratio	Mean	S.D	Unpaired 't' test	p value
Benign Rx Ultrasound	2.80	0.86	t = 10.932	p<0.001**
Malignant Rx Ultrasound	5.86	0.86		
	Mean SD)	3.82 (0.74)		
	Median	3.97		
	Range	1.2-7.9		

The mean strain ratio is 5.86 ± 0.86 for malignant lesions and 2.86 ± 0.86 for benign lesions. This difference shows statistically significant (P value <0.001). The statistical analysis done by using Unpaired' test (value of 10.932) shows statistically significant (P value <0.001) as shown in table 6. The sensitivity of strain ratio is 81.4%, specificity of 83%, positive predictive value 88.4%, negative value 83.5% and accuracy of 91.5% with cut-off point of 5 between benign and malignant lesions as shown in table 7.

Table 7 Diagnostic efficacy of Elastography grade, strain ratio and combination of both parameters vs histopathology in diagnosing the lesion of prostate

Histopathological diagnosis vs	Sensitivity (%)	Specificity (%)	Positive Predictive value (%)	Negative Predictive value (%)	Accuracy (%)
TRUS	76.1%	88%	78.6%	71.5%	88.33%
ELASTOGRAPHY GRADE	76.5%	81%	78.6%	71.5%	77.8%
STRAIN RATIO	81.4%	83%	88.4%	83.5%	91.5%
(Elasto + Strain)	85.71%	89.3%	91.25%	94.6%	91%

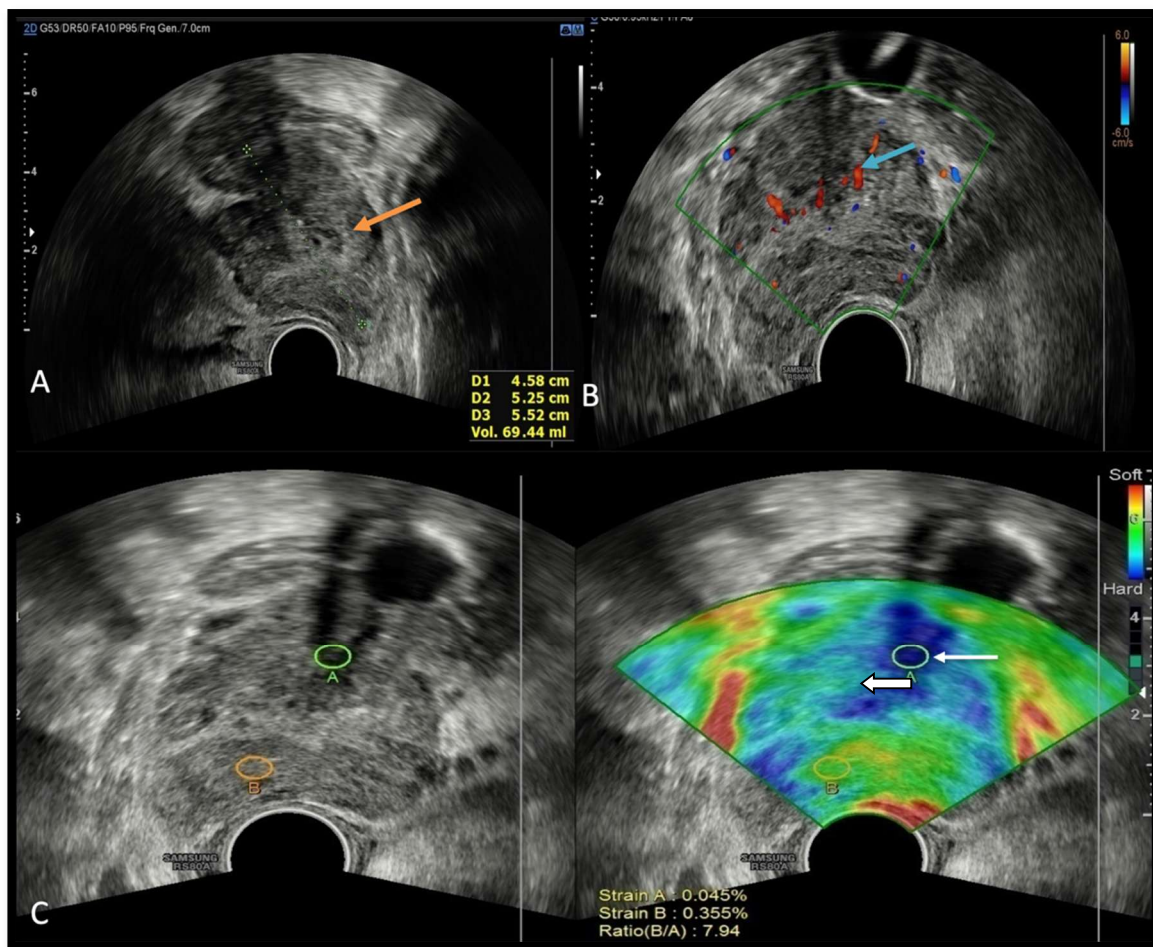


Figure 3 A 56 yr. old male complaints of increase frequency of micturition and dysuria A) On transrectal B mode ultrasound prostate measures 69.44 cc and appears enlarged in size (red arrow) with increased vascularity (B) is noted at the junction of transitional and peripheral zone indicated by arrow (blue arrow) . There is heterogeneous echogenicity noted at this junctional zone. (C) On elastography the arrow (white arrow) indicates the hypoechoic lesion shows stiffness in the centre of the lesion and strain at the periphery (periphery of the lesion in green and the central part in blue). Elastography Grade IV. SV ratio is 7.94 suggestive of malignancy. Histopathology features suggestive of Adenocarcinoma. Gleason's score is 3+3

The maximum number of cases were 10(16.7%) out of 19 cases having Gleason score of (3+4)7 followed by 6(3+3) in 5(8.3%) cases which is then followed by score of 8(4+4) in 4(6.7%) cases as shown in table 8.

Table 8 Distribution of Gleason score of study subjects

Gleason’s score	Frequency (n)	Percentage (%)
3 + 3	6	8.3%
3+ 4	10	16.7%
4 + 4	4	6.7%
Total	19	100%

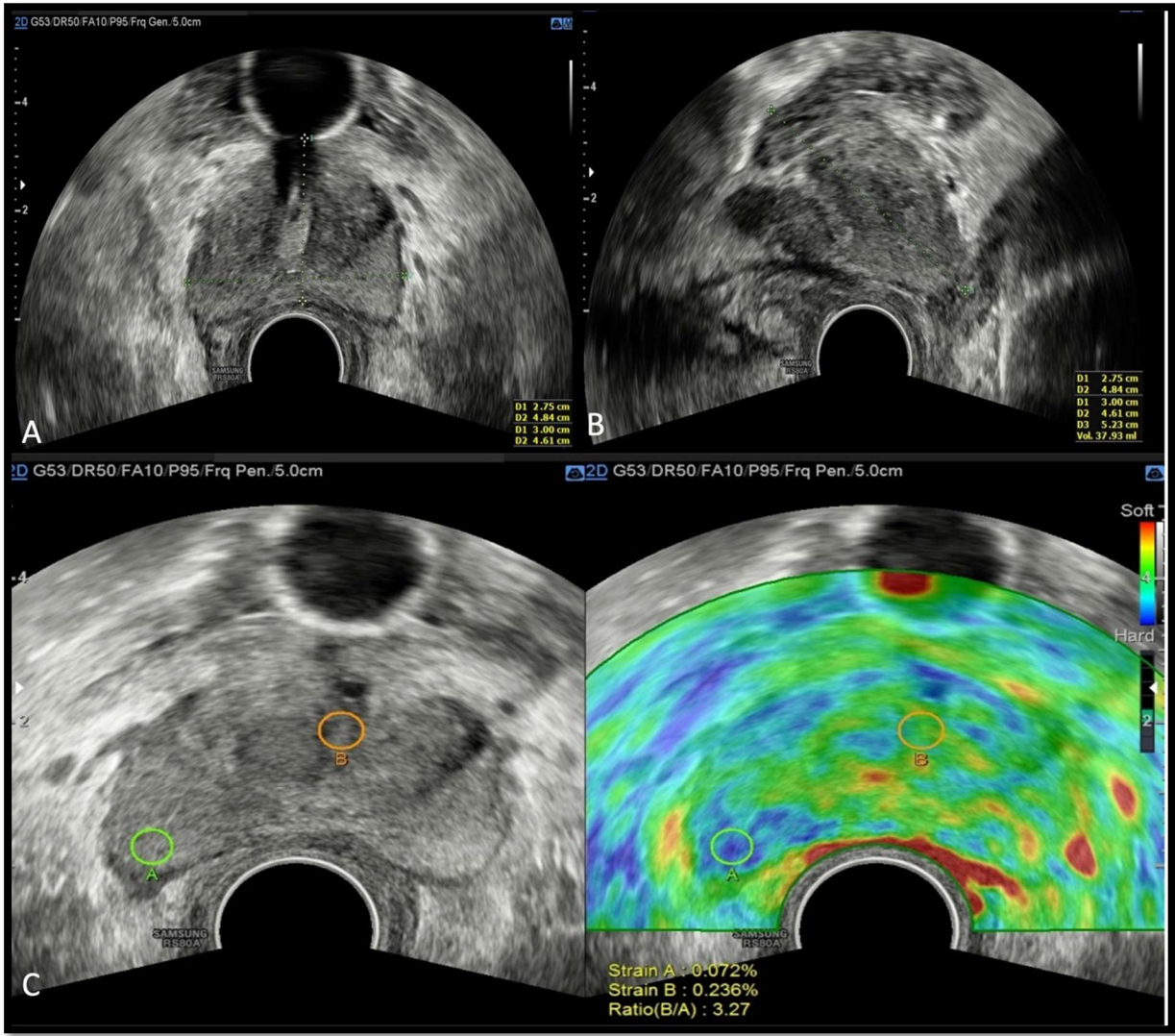


Figure 4 49 yr. old male complaints of lower urinary tract symptoms since 2 months.(A&B) : On TRUS prostate measures 37.93cc and appears enlarged in size and shows heterogeneous echo texture.(C) On elastography shows symmetric strain which is heterogeneous (mosaic and symmetrical pattern of blue and green). Elastography Grade II. SV ratio is 3.27. Histopathology: Benign prostatic hypertrophy.

4. DISCUSSION

The current investigation analysed 60 individuals with increased PSA, abnormal findings on digital rectal examination, and additional targeted biopsies from aberrant locations revealed by transrectal real-time elastography and transrectal ultrasound. The findings of each of the abovementioned modalities were compared to histological diagnosis. The patients in our research varied in

age from 37 to 86 years. The majority of patients in our research were above the age of 60 (60 %). The Mean value of age (years) of our study subjects was 67.81 ± 9.32 with median (IQR) of 69.82 (61.2-75.9) and range of 37-86.

In our study 18 lesions were malignant and 42 lesions are benign. All the malignant lesions turn out be adenocarcinoma of prostate on histopathology. The study conducted by (Hung et al., 2013) correlated the synergistic effect of prostatitis in both BPH and cancer. Both prostatitis and benign prostatic hyperplasia are synergistically related with prostate cancer; however benign prostatic hyperplasia is a considerably larger risk factor for prostate cancer than prostatitis. In our study 12(20%) out of 60 patients were presented with acute prostatitis. 22(36.7%) out of 60 patients were presented with chronic prostatitis. Remaining 3(5%) out of 60 patients were presented with mixed prostatitis.

The mean PSA (ng/mL) level in our research sample is 39.2 11.76, with a median (IQR) of 41.54. (2.57-112.2). According to Thompson et al., (2004) and Schröder et al., (2008), individuals with benign prostatic hypertrophy (BPH) and inflammatory diseases (acute and chronic prostatitis) would also have a PSA level more than 4 ng/mL. The mean PSA (ng/mL) level for malignancy in our research group was 55.23 with a standard deviation of 29.98, whereas the mean PSA (ng/mL) level for benign conditions was 7.43 with a standard deviation of 4.16. Similarly in our study mean value mean of PSA density (ng/cm³) of study subjects is 0.631 ± 0.248 with median (IQR) of 0.714(0.05-3.33). However the study done by Mottet et al., (2017) and Nordström et al., (2018) the cut- off used most commonly is 0.15 or 0.20 ng/mL. This calculation however has many potential sources of error such as volume calculation and sampling bias. In our study the mean PSA density (ng/cm³) level for benign conditions was 0.28 ng/mL with a standard deviation of 0.46 and for malignancy was 1.38 with a standard deviation of 0.73.

The total mean prostate size in our sample is 44.2 6.5, with a median (IQR) of 42.87. (30-65). Huang Foen Chung et al., (2004) observed that as the prostate volume increases, the risk of prostate cancer increases significantly, even when the prostate is enlarged in both benign prostatic hypertrophy (BPH) and prostate cancer. The mean size of the prostate in our research cohort was 47.68 cm³ with an 8.63 standard deviation for malignancy and 42.6 cm³ with a 5.68 standard deviation for benign conditions. We employed 12-core systematic biopsy in all patients in our trial, as (Levine *et al.*, 1998) research found that employing a 12-core biopsy significantly enhanced prostate cancer detection when compared to normal sextant biopsy.

Transrectal ultrasonography revealed 29 (48.3 %) patients with uniform echogenicity, 19 (31.7 %) cases with hypo echogenicity, and 12 (%) cases with hyperechoic echogenicity in our investigation. 23 lesions had enhanced vascularity on colour Doppler ultrasonography, whereas 37 lesions had normal vascularity. Applewhite et al., (2001) described the ultrasonography appearance of prostatic tumours. TRUS alone is ineffective in detecting prostate cancer. While some disease manifests as hypoechoic regions that may clearly be distinguished from normal homogeneous areas, the majority of hypoechoic lesions are benign. Additionally, some tumours seem hyperechoic, whereas many early neoplastic cases appear isoechoic, indistinguishable from surrounding normal prostate gland tissue. TRUS has a positive predictive value of 78.57 percent and a negative predictive value of 81.25 percent in our research sample. TRUS was used to identify 21 lesions indicative of cancer. Sixteen (76.2 percent) of these twenty-one instances were appropriately recognised as cancer, whereas five (23.8 %) were benign lesions. TRUS failed to detect 5 (23.8%) malignant lesions that were later determined to be benign. TRUS had a sensitivity of 76.1 percent and a specificity of 88 percent in our analysis, but in (Terris *et al.*, 1991) investigation, TRUS had a sensitivity of 53.3 % and a specificity of only 75%.

The strain ratio was employed in our research; the mean strain ratio for malignant lesions was 5.86 ± 0.86 whereas the mean strain ratio for benign lesions was 2.86 ± 0.86 . This discrepancy is statistically significant ($P < 0.001$). El Fattah Hassan Gadalla et al., (2015) found that using the strain ratio parameter to evaluate elastography images results in a greater sensitivity of 74.2 %, specificity of 73.7 %, and accuracy of 74.0 % between benign and malignant lesions at an optimum cut-off point of 5.5. The statistical analysis conducted in our research revealed that the Unpaired' test (value of 10.932) is statistically significant (P value 0.001). At a cut-off point of 5, our research found a greater sensitivity of 81.4 %, a higher specificity of 83 %, and a higher accuracy of 91.5 % between benign and malignant lesions.

Similarly, Zhai et al., (2012) determined a cut off of 3.05, which is similar to our research, however Zhang et al., (2012) determined a cut off of 17.44, which is significantly different from our data. According to our results, real-time elastography may be employed effectively to improve the degree of confidence in distinguishing benign from malignant disease, hence avoiding needless biopsies.

5. CONCLUSION

Prostate ultrasound elastography, based on our findings, may be a valuable technique for detecting malignant and benign tumours. Additionally, it may aid in identifying the biopsy site; however, a more thorough review by a larger research is recommended.

Abbreviations

BPH (Benign prostatic hyperplasia), CT (Computed tomography), DRE (Digital rectal examination), HPE (Histopathological examination), MRI (Magnetic resonance imaging), PSA (prostatic specific antigen), TRUS (Transrectal ultrasound), TURP (Transurethral resection of prostate), USG (Ultrasonography) and SV (Strain ratio)

Acknowledgement

We are indebted to the participants for making this research possible and to all physicians, faculty and junior residents of radiology department and staff of NKP Salve Institute of Medical Sciences and Research centre, Dighodh hills, Nagpur 440019, Maharashtra, India.

Contributions of Authors

All authors made significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; contributed to the writing of the article or critically revising it for important intellectual content; gave final approval of the published version; and agree to be accountable for all aspects of the work.

Ethical considerations

The research received ethical clearance from the institutional ethics committee. At all phases of the trial, data were kept anonymous and confidential.

Funding

This study has not received any external funding.

Conflicts of interest

The authors declare that there are no conflicts of interests.

Data and materials availability

All data associated with this study are present in the paper.

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